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10/560,092	12/09/2005	Jose Luis Castro Pineiro	T1633P	9516

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EXAMINER	
CARTER, KENDRA D	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,092	PINEIRO, JOSE LUIS CASTRO	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/9/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 14-23 are pending. Claims 21-23 are withdrawn from consideration.

Election/Restrictions

Applicant's election with traverse of Group I, claims 14 in part – 20, in the reply filed on March 26, 2007 is acknowledged. The traversal is on the ground(s) that the ability to treat or prevent a disease associated with deposition of ABeta which is found among the compounds provides unity of invention and a common link among the groups, thus facilitating examination. Additionally, no serious burden for examination is present if restriction is not required. This is not found persuasive because the common technical feature in all groups is a growth hormone secretagogue. This element cannot be a special technical feature under PCT Rule 13.2 because the element is shown in the prior art. In particular, Draper et al. (US 5,767,124) discloses a growth hormone secretagogue (see title and abstract, lines 1-5). As a result, no special technical features exist among the different groups because the inventions in Groups I to VII fail to make a contribution over the prior art with respect to novelty and inventive step. In conclusion, there is a lack of unity of inventions, and therefore restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(1) Claims 14-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a disease associated with deposition of AB in the brain, does not reasonably provide enablement for preventing a disease associated with deposition of AB in the brain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treating or preventing a disease associated with deposition of AB in the brain comprising administering a growth hormone secretogogue in combination with a compound which inhibits

the secretion of AB. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method of treatment or prevention of a disease associated with deposition of AB in the brain comprising administering to a patient in need thereof a therapeutically effective amount of a growth hormone secretogogue in combination with a therapeutically effective amount of at least one agent which modifies the production or processing of AB in the brain, said agent being selected from: compounds which inhibits the secretion of AB...."

(2) The breadth of the claims:

Claims 14-20 embraces preventing a disease associated with deposition of AB in the brain comprising administering a growth hormone secretogogue in

combination with a compound which inhibits the secretion of AB. This reads on completely preventing diseases associated with deposition of AB in the brain. The specification does not enable the prevention of any disease associated with deposition of AB in the brain.

(3) The state of the prior art:

The state of the art regarding completely preventing diseases associated with deposition of AB in the brain is low or do not exist.

(4) The predictability or unpredictability of the art:

The predictability of preventing diseases associated with deposition of AB in the brain is relatively low. Therefore, to one skilled in the art, completely preventing diseases associated with deposition of AB in the brain is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to preventing diseases associated with deposition of AB in the brain is completely lacking. The specification as filed does not speak on or show any working examples any

studies performed that prevent diseases associated with deposition of AB in the brain. The specification states that for the prevention of Alzheimer's disease (AD), the growth hormone secretagogue (GHS) and amyloid modifier may be dosed at the levels which are effective for the original purposes of the separate compounds. Thus, the GHS will typically be dosed at levels known to provide increased secretion of endogenous growth hormone in a human subject, and the amyloid modifier at levels known to cause significant inhibition of secretion of AB. In many cases, these dosage levels are available from the published literature, but otherwise are readily determined by standard clinical methods (see page 24, last paragraph in its entirety). Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on preventing disease associated with deposition of AB in the brain. As discussed above the specification fails to provide any support for completely preventing disease associated with deposition of AB in the brain. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. In particular, the prior art cited by the applicant does not show the complete prevention of diseases associated with deposition of AB in the brain by administering a combination of both compounds. One would need to provide data that the patient was administered the combination of both compounds and never had deposition of AB in the brain.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating diseases associated with deposition of AB in the brain, but not for the prevention.

(2) Claims 14-17 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the growth hormone secretagogue of formula I in combination with a compound which inhibits the secretion of AB of formula XI(a) or XII, does not reasonably provide enablement for all growth hormone secretagogue compounds and all compounds which inhibit the secretion of AB. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of treatment a disease associated with deposition of AB in the brain comprising administering a growth hormone secretogogue in combination with a compound which inhibit the secretion of AB. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to

In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 1 is drawn to "a method of treatment or prevention of a disease associated with deposition of AB in the brain comprising administering to a patient in need thereof a therapeutically effective amount of a growth hormone secretogogue in combination with a therapeutically effective amount of at least one agent which modifies the production or processing of AB in the brain, said agent being selected from: compounds which inhibits the secretion of AB...."

(2) The breadth of the claims:

Claims 14-17 and 19 embraces and reads on treating a disease associated with deposition of AB in the brain comprising administering all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB. The specification does not enable the treatment of diseases

associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB.

(3) The state of the prior art:

The state of the art regarding treating diseases associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of ABis low or do not exist.

(4) The predictability or unpredictability of the art:

The predictability of treating diseases associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibits the secretion of AB is relatively low. Therefore, to one skilled in the art, treating diseases associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB is highly unpredictable.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to the treating a disease associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that treat diseases associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB. The specification states that for the treatment of Alzheimer's disease (AD), the growth hormone secretagogue (GHS) and amyloid modifier may be dosed at the levels which are effective for the original purposes of the separate compounds. Thus, the GHS will typically be dosed at levels known to provide increased secretion of endogenous growth hormone in a human subject, and the amyloid modifier at levels known to cause significant inhibition of secretion of AB. In many cases, these dosage levels are available from the published literature, but otherwise are readily determined by standard clinical methods (see page 24, last paragraph in its entirety). Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02.

(7) The quantity of experimentation necessary:

The instant claims read on treating a disease associated with deposition of AB in the brain with all growth hormone secretogogues in combination with all compounds which inhibit the secretion of AB. As discussed above the

specification fails to provide any support for treating a disease associated with deposition of AB in the brain with all growth hormone secretogogue in combination with all compounds which inhibit the secretion of AB. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation. In particular, the effective dosing of a combination of both compounds to treat diseases associated with deposition of AB in the brain would require one skilled in the art to perform clinical tests. The specification states that the dosage of the GHS of formula I and the compound which inhibit the secretion of AB may be contemplated (see page 25, paragraph 3, line 3 and paragraph 4, line 5), which reads on the possibility of the effectiveness of the dosage amounts of each compound. In order to find the effective dosage range for the combination of all growth hormone secretogogue in combination with all compounds which inhibit the secretion of AB would require undue experimentation. Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for treating a disease associated with deposition of AB in the brain with the growth hormone secretagogue of formula I in combination with a compound which inhibits the secretion of AB of formula XI(a) or XII.

(3) Claims 14-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A written description on the treatment of a disease associated with deposition of AB in the brain with the specific administration of a therapeutically effective amount of a growth hormone secretagogue in combination with a therapeutically effective amount of a compound which inhibits the secretion of AB is not described in the specification. The current specification discloses that for the treatment of Alzheimer's disease (AD), the growth hormone secretagogue (GHS) and amyloid modifier may be dosed at the levels which are effective for the original purposes of the separate compounds. Thus, the GHS will typically be dosed at levels known to provide increased secretion of endogenous growth hormone in a human subject, and the amyloid modifier at levels known to cause significant inhibition of secretion of AB. In many cases, these dosage levels are available from the published literature, but otherwise are readily determined by standard clinical methods (see page 24, last paragraph in its entirety). The above description provides for the treatment with the individual compounds but

not for the combination of the two compounds, especially, since synergistic interaction is disclosed (see page 25, line 2). No data or examples are given to provide one skilled in the art to reasonably use the invention to treat diseases associated with deposition of AB in the brain.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shearman et al. (US 2006/0241133 A1) in view of Churcher et al (WO 03/018543 A1).

Shearman et al. teaches the applicant's elected compound for a growth hormone secretagogue for the treatment of age-related cognitive decline or mild cognitive impairment (see abstract in its entirety; addresses claims 14 in part, 16 and 18) who additionally possesses one or more risk factors for developing Alzheimer's disease selected from: a family history of the disease; a genetic predisposition to the disease; elevated serum cholesterol; adult-onset diabetes mellitus; raised CSF levels of total tau; raised CSF levels of phosphor-tau; and lowered CSF levels of AB42 (see page 3, paragraph 26 in its entirety; addresses claims 15 and 17).

Shearman et al. does not teach a compound which inhibits the secretion of AB, particularly the Applicant's elected compound (claims 14 in part and 19 and 20).

Churcher et al. teaches the Applicant's elected compound for the γ-secretase inhibitor (see page 20, example 2) to treat Alzheimer's disease (see abstract.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Shearman et al. and the Applicant's elected compound for the γ-secretase inhibitor because of the following: (1) both Shearman et al. and Churcher et al. teach methods to treat Alzheimer's disease; (2) "It is *prima facie* obvious to combine two compositions

each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992); and *In re Geiger*, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KDC

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